A I D S TREATMENT N E W S

Issue Number 386
December 20, 2002

Published 18 times a year by
John S. James
AIDS Treatment News
1233 Locust St., 5th floor

Contents

AIDS Treatment News

Subscription and Editorial Office:
AIDS Treatment News
Philadelphia FIGHT
1233 Locust St., 5th floor
Philadelphia, PA 19107
800-TREAT-1-2 toll-free U.S. and Canada
fax: 215-985-4952
email: aidsnews@aidsnews.org

Editor and Publisher: John S. James
Associate Editors: Jennifer Cohn, Tadd T. Tobias, R.N.
Reader Services: Allison Dinsmore

Statement of Purpose:
AIDS Treatment News reports on experimental and standard treatments, especially those available now. We interview physicians, scientists, other health professionals, and persons with AIDS or HIV; we also collect information from meetings and conferences, medical journals, and computer databases. Long-term survivors have usually tried many different treatments, and found combinations that work for them. *AIDS Treatment News* does not recommend particular therapies, but seeks to increase the options available.

Subscription Information: Call 800-TREAT-1-2

Businesses, Institutions, Professional offices: $325/year. Includes early delivery of an extra copy by email.

Nonprofit community organizations: $150/year. Includes early delivery of an extra copy by email.

Individuals: $140/year, or $80 for six months.

Special discount for persons with financial difficulties: $54/year, or $30 for six months. If you cannot afford a subscription, please write or call.

Outside the U.S., Canada, or Mexico, add airmail postage of $20/year, or $10 for six months.

Back issues, and discounts for multiple subscriptions, are available; contact our office for details.

Please send U.S. funds: personal check or bank draft, international postal money order, or travelers checks. VISA, Mastercard, and purchase orders also

housing there, you must complete the housing process by January 10 to prevent your registration from being cancelled.

New Government AIDS Web Site, Phone Number.....

A new site, www.aidsinfo.nih.gov, has government-approved treatment information, as well as searchable listings of government and private clinical trials.

Smallpox Vaccination Begins in U.S. -- Precautions Needed

by John S. James

On December 13 President Bush announced that the U.S. will begin a smallpox vaccination program. It will be mandatory for about 500,000 military personnel, with voluntary but recommended vaccination for over 400,000 civilian health-care workers most likely to encounter smallpox in case it is spread deliberately. A few in the military started receiving the vaccine immediately; the program for civilian health workers may start in January. Eventually, vaccination might be recommended for as many as 10 million health and emergency workers in the U.S.

People with HIV or certain other medical conditions -- probably millions of Americans -- cannot be vaccinated safely because the vaccine uses a live virus, called vaccinia. Vaccinia can cause a dangerous infection, especially in persons with immune deficiencies. Persons at risk from vaccination need to be aware of other precautions as well, since one can get this infection not only by being vaccinated, but also by close contact (especially household

contact) with someone who has been vaccinated within about three weeks. Vaccinia can be spread by contact with someone's vaccination site, or contact with materials that have touched the site. If vaccinia infection does occur, there are recommended treatments -- VIG (vaccinia immune globulin), and cidofovir, an approved drug that can have serious side effects -- but the infection can be fatal despite treatment. Hospitals are concerned that their healthcare workers who get vaccinated could infect patients, many of whom have immune deficiencies. Some hospitals may send vaccinated staff home during the two to three weeks they could be contagious, some may decide just to keep them out of certain wards, and a few have refused to participate in the national vaccination program.

In case of actual exposure to smallpox, or cases found anywhere in the world, vaccination might be worth the risk even for many who would otherwise be screened out. Fortunately, vaccination does protect against smallpox even if it is given shortly after exposure (in the first three days if possible). Therefore most people can wait, and decide about vaccination only if a smallpox outbreak occurs.

New kinds of smallpox vaccines are being tested. Some of them may be safe enough for many people with HIV or others who should not get the current one.

A much smaller program is starting in England, vaccinating about 300 healthcare workers against smallpox. Israel recently vaccinated about 17,000 medical and rescue workers in preparation for a U.S. war on Iraq -- apparently with little problem from side effects. We have not heard of smallpox vaccination plans in other countries.

For More Information

The U.S. government is planning a massive public education campaign about smallpox vaccination. This information is being prepared by leading experts and will probably be the best available. Until it is ready, those wanting recent information can check the following. (Note: We published these links on December 23, 2002. Be sure to look for more recent information.)

* On December 13 the White House issued a question-and-answer document about the vaccination program; it is at:
http://www.whitehouse.gov/news/releases/2002/12/20021213-3.html

* The American Public Health Association published an interim policy statement at:
http://www.apha.org/legislative/policy/smallpox.htm
and a press release on the new White House plan at:
http://www.apha.org/news/press/2002/smallpoxresponse.htm

* The *New England Journal of Medicine* is publishing several articles about smallpox in the January 30, 2003 issue, but has released them early at:
http://nejm.org/earlyrelease/early.asp

* Three articles in the December 20 *Science* (these require a subscription or payment to read online):

"Rough-and-Tumble Behind Bush's Smallpox Policy,"
http://www.sciencemag.org/cgi/content/summary/

298/5602/2312?etoc

"Treating Vaccine Reactions: Two Lifelines, But No Guarantees," http://www.sciencemag.org/cgi/content/summary/298/5602/2313?etoc

"Looking for Vaccines That Pack a Wallop Without the Side Effects," http://www.sciencemag.org/cgi/content/summary/298/5602/2314?etoc

* *JAMA (Journal of the American Medical Association)* recently published an article on the risk of getting an infection from someone who has recently been vaccinated; see "Contact Vaccinia -- Transmission of Vaccinia from Smallpox Vaccination," October 16, 2002. Note that this article is based on experience from before the HIV epidemic.

* For detailed practical information see The Military Vaccines Web Site: http://www.vaccines.army.mil/smallpox.asp

Comment

So far the vaccination program is mostly getting good medical reviews. Public health experts are especially relieved that it is not trying to vaccinate the whole population, as some had proposed.

No one knows the risk of an attack. The case for the program is that if smallpox does occur, there will be teams already vaccinated and ready to respond -- and equally important, some current experience in large-scale vaccination and a program that is ready to go, allowing many more people to be protected quickly if necessary. The U.S. already has enough doses to vaccinate everyone in the country, even before new vaccine is manufactured.

The world is not as lucky. "Last year epidemiologists were very concerned to learn that the WHO's vaccine safety net of 200 million doses had been destroyed in the late 1980s when the United States withheld funds and the agency was unable to pay $50,000 to refrigerate the supply." (Lawrence Brilliant, M.D., "Are We Safe? Halting the Next Plague," *The Oprah Magazine*, June 2002.)

It is strange to plan for smallpox in a vacuum, disconnected from how we got into this situation or how to avoid it in the future. But the vaccination program is a fact, and everyone with HIV or certain other medical conditions will need to consider precautions.

Be sure to get the latest information. This article, published in late December 2002, will soon be obsolete.

U.S. Blocks Trade Agreement on Generic Drug Access in Poor Countries

by John S. James

On December 20, international trade talks in Geneva, Switzerland failed to resolve the major remaining issue on access to generic versions of patented medicines in developing countries to meet public-health needs. All 143 other countries were ready to accept a compromise text negotiated on December 16. But the U.S. insisted on an additional restriction -- to limit the agreement to AIDS, tuberculosis, malaria, and similar major epidemics. Cancer, heart disease, asthma, and hundreds of other illnesses would have been excluded. Developing countries

would not accept this restriction, and European countries did not want to re-open the difficult negotiations.

All treatment activists we have heard from think that the compromise, which was reluctantly agreed to by poor countries, would have been harmful. They feared that it would create a cumbersome process, easily open to obstruction, that would rarely or never be used to help anyone obtain medicine, while damaging some of the understandings in place. Some feared it could threaten or even end the historic consensus reached last year by the world's governments that trade rules should not be an obstacle to public health. Negotiations will start again in early 2003, attempting to reach agreement by February 11.

Background

Traditionally patent laws were decided separately by each nation, not by international organizations. And until about 1995, while patents on pharmaceuticals were widely recognized among rich countries, they were not uniformly binding on developing countries. But starting with the World Trade Organization (WTO) treaty in 1995, almost every country on Earth was pressured to sign on to a set of trade rules that included pharmaceutical patents. These rules established deadlines for developing countries, and required full compliance by 2006 (later extended to 2016 for least-developed countries). Patent holders can set whatever price they want, and apparently no thought was given to the fact that major corporations would regularly price life-critical new drugs totally out of reach of most of the world's people.

Current WTO rules allow a country to override a patent to meet a legitimate public need, under certain conditions, through a mechanism called compulsory licensing. But within a few years the existing rules may block export for compulsory licensing, stopping its use in any country not big enough and rich enough to have its own domestic pharmaceutical industry. The Geneva negotiations that just failed were called to deal specifically with this production-for-export problem.

In November 2001 in Doha, Qatar, all the countries in the trade negotiations agreed that WTO rules would not prevent countries from taking measures to protect public health (the United States reluctantly signed on in order to keep the negotiations moving). Developing countries were promised that the export problem would be corrected in 2002, presumably in accordance with the Doha agreement. But several rich countries -- the U.S., Canada, Japan, the European Union, and Switzerland -- pushed for restrictions on behalf of their pharmaceutical companies. Developing countries this month were pressured to accept these harmful restrictions. But they drew the line at caving in to the disease limitation finally demanded by the United States.

Shortly after rejecting the agreement, the U.S. said it would not bring action against certain drug exports while the talks continued. This statement was widely seen as a public-relations move unlikely to have any practical effect. For generic manufacturers must get drug approvals in each country, and deal with other time-consuming and expensive obstacles as well, before export can happen. They need stability and are unlikely to base business decisions on a

unilateral statement designed to look good, but that can be taken back any time.

For more information see news reports in the *Washington Post* ("Talks on Low-Cost Drug for Poor Nations Stall," by Paul Bluestein, December 21), *The New York Times* ("Trade Talks Fail to Agree on Drugs for Poor Nations," by Elizabeth Becker, December 21), *The Guardian* (UK) ("U.S. Wrecks Cheap Drugs Deal," by Larry Elliott and Charlotte Denny, December 21 -- which reported that Vice President Cheney apparently made the decision not to accept the compromise), *The Wall Street Journal* ("U.S. Retreats from Earlier Move to Keep Drugs from Poor Nations," by Michael M. Phillips, December 23), or other newspapers and wire services. For a more detailed description of the negotiations see *Inside U.S. Trade* ("TRIPS Draft Strikes Balance on Many Issues, but Isolates U.S. on Scope," December 20).

Quotes

"We're basically talking about a system that could help save millions. If a good system isn't created, you can imagine a world a few years from now where multinational companies control the patents for everyone." (Ellen 't Hoen of Doctors Without Borders, quoted in *The New York Times*, December 21.)

"President Bush wants to argue that the diseases American children receive treatment for are off limits to poor children in poor countries, but they cannot win that argument." (James Love, director of the Consumer Project on Technology, quoted in *The New York Times*, December 21).

"You have to ask yourself, are you going to have a patent system or not? If you're going to permit people to import drugs to treat cancer, diabetes and heart disease, what are you going to do when someone says, I want Viagra on the list?" (Unnamed U.S. trade official, quoted in the *Washington Post*, December 21.)

Comment: Issues Needing Attention

* Pharmaceutical patents are unique in ways that need more recognition. For example, they rely on human trials where patients may risk their health or even their lives to test an experimental drug. And if the trial is successful, it cannot be repeated for another drug for the same illness, as that would involve giving people a treatment then known to be less than the standard of care. Vaccines in particular may be tested in thousands of people; once they are known to work, how could a similar vaccine ethically be tested on other thousands? In addition, patents today often claim natural substances that are part of the human body, for which there may be no biological workaround. And needless to say, medical patents are more likely than others to be life-critical.

We do not argue that pharmaceutical patents should be abolished, but that they involve unique social responsibilities -- which the multinational corporations have so far largely dismissed. If industry continues to obstruct instead of helping to build systems that work for people, it is our duty as citizens (of the United States especially) to prevent our government from being used as a tool by irresponsible corporations to bully others.

* The Geneva negotiations that failed in 2002 will continue in 2003, writing rules that may become law all over the world for years to come. In developing these rules, everyone needs to be aware that we are near the beginning of an era of unprecedented progress in medicine. So far the great advances in biological understanding have been poorly translated into practical treatments, but that will change. Imagine the consequences if penicillin and all other antibiotics had been denied to most of the world for ten to 20 years for intellectual-property reasons; then imagine this happening again and again in cancer, Alzheimer's, diabetes, and other major diseases.

* Patent or no patent, companies are not interested in regions too poor to support a lucrative market. And in the poorest countries, most people cannot pay even generic prices out of pocket. What patents do in these areas is to deprive both governments and non-governmental organizations of tools they need to reduce the burden of disease -- with little or no compensating benefit to anyone. Trade negotiators, in seeking "balance" between pharmaceutical companies and poor people needing treatment, may have overlooked the extent to which the world's richest companies can litigate a molehill into a mountain.

* Patents might conceivably be made to work in poor countries, with successful drugs being licensed to international agencies for regional or worldwide use. But this possibility remains unproven so far.

* Drug patents are said to support public interest by creating incentive for innovation. This is true in rich countries, but the full truth is more interesting. Pharmaceutical corporations do pay for expensive clinical trials, but otherwise do much less science than generally believed. They are primarily marketing organizations.

* For a report on how patent misuse seriously blocks research, see "Drug Abuse: Where Have All the New Meds Gone?" in *The New Republic*, October 7, 2002. For example, it noted that Bristol Myers Squibb was not working on over 50 proteins that might be involved in cancer, "because the patent holders either would not allow it or were demanding unreasonable royalties." The article is currently online at:
http://www.biohope.org/media/article.cfm?articleid=3054&state=na

* Another major cause of the disappointing progress in translating huge scientific advances into practical treatment progress is that medical research is mostly divided between academics interested in pure science and corporations interested in pure profit. Research also needs a middle ground. It needs top scientific teams committed to practical results, but allowed to develop anything they choose in order to advance human health, and to communicate freely about their work. Then they can look for the best opportunities anywhere in their field of competence, instead of being caged into some corporate purpose that might not have a good path forward just then -- or being stuck in an academic environment where they can do basic science and publish their findings, but not develop them for human health.

We can begin reform by asking researchers what real obstacles they face, what support they need to be

effective, and how the systems must be changed.

* It should be unthinkable that thousands of people die every day because they cannot afford the medicines they need -- in part because of government rules made to "balance" their interests against those of a handful of huge corporations that contribute lavishly to politicians, think tanks, and other "thought leaders." We had thought there was consensus for change. But this is the Age of Abuse, and the consensus did not include Washington. Clearly millions in the U.S. alone would object if they understood, yet not one in a thousand of them has ever made their voice heard on this matter. Activists must do much better in preparing this issue so that not only specialists but also people anywhere can pick it up and run with it.

Tenofovir (Viread®) Access for Poor Countries

by John S. James

On December 17 Gilead Sciences announced that it would make its antiretroviral (tenofovir disoproxil fumarate, brand name Viread) available at cost to qualified organizations providing HIV treatment in all 53 nations in Africa, and 15 additional countries classified as "least developed" by the United Nations. The company said the program would be running by the second quarter of 2003. Information and technical assistance in applying for and using the drug will also be provided.

Also, Gilead will participate in the 3,000-patient Development of Antiretroviral Therapies (DART) study, sponsored by the UK's Medical Research Council, which will begin in 2003 in Uganda and Zimbabwe, to evaluate antiretroviral treatment strategies where resources are limited. In addition it is studying tenofovir to prevent transmission of HIV.

The text of the press announcement is at: http://www.gilead.com/wt/sec/pr_1040081128. For more information about the drug, see http://www.viread.com.

Comment

Tenofovir is an important drug because it is easy to use (one pill per day), has less problem with side effects than most antiretrovirals, and leads to relatively slow development of HIV drug resistance. However, side effects and drug resistance do occur -- and resistant virus is likely to be cross-resistant to AZT and to some other HIV drugs as well. So when used to treat existing HIV infection, tenofovir must be combined with other antiretrovirals to reduce this resistance.

This is not the only program to provide an antiretroviral at cost in some poor countries. It may be better designed than some of the others, in reducing cumbersome country-by-country negotiation and administration.

There are some concerns. "At cost" can translate to several times the price at which a generic manufacturer could sell the same drug at a profit. This is because proprietary pharmaceutical companies have so high a profit margin on each pill sold that they have little incentive to automate production efficiently. Also, accounting practices can differ greatly, including which